IL-1 Receptor Antagonist Rescues Chondrocytes From Cellular Death Following Intra-Articular Fractures in a Porcine Pilon Fracture Model

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Purpose: Our objective was to investigate the percentage of chondrocytes undergoing apoptosis or necrosis on both the tibial plafond and talus at 24 and 48 hours following high-energy pilon fractures and if an interleukin (IL)-1 receptor antagonist (IL-1ra) can rescue chondrocytes from cellular death.

Methods: Of 14 porcine hindlimb hocks, 4 hindlimb hocks were used as controls, 5 were used as fracture models, and 5 underwent fracture with treatment of 150 ng/ml of IL-1ra. For each limb, 2 chondral samples were taken from the tibial plafond and the talus, within 5 mm of the fracture. Samples were processed at 24 hours and 48 hours with Hoechst 33342 as a counter stain, FAM FLICA Caspase-1 probe for apoptosis, and 7-aminoactinomycin D (7-AAD) for necrosis. Confocal microscopy and subsequent cell counting were performed. Data were analyzed via analysis of variance with Tukey post hoc test.

Results: All control samples had chondrocyte survival rates >94%, necrosis rates <5%, and apoptotic rates <2%. All fracture models had significantly lower chondrocyte survival rates than the controls, while all treatment groups had greater survival rates than the fracture models. At 24 hours, chondrocyte death was driven by necrosis (39%-45%), while apoptosis increased from 4%-7% at 24 hours to 15%-18% at 48 hours. At 48 hours both the talus and plafond fracture groups had the lowest chondrocyte survival rates (23% [0.09] and 27% [0.12]), which was significantly lower than the 24-hour fracture groups (51% [0.03], $P<0.001$ and (53% [0.24]). The treatment group had significantly increased survival rates, with talus and plafond fracture group survival rates at 24 hours (0.80% [0.12], 0.82% [0.06]), and 48 hours (0.77% [0.06] and 0.71% [0.05]).

Conclusion: Early chondrocyte death is driven by necrosis, with apoptosis beginning at 48 hours. IL-1ra markedly increased chondrocyte survival rates 24 and 48 hours following pilon fractures.